PATENT

Thereby certify that on the date specified below, this correspondence is being deposited with the United States Postal Service as Express Mail in an envelope addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Mars 29, 2006

Date

Kay Bulen

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant

: Tim Hui-Ming Huang

Application No.

: 10/081,327

Filed

: 02-21-2002

For

: HIGH-THROUGHPUT METHODS FOR DETECTING DNA

METHYLATION

Examiner

: Jeanine Anne Goldberg

Art Unit

: 1634

Docket No.

: 40629-2

Date

: March 29, 2006

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT

Dear Commissioner:

In accordance with 37 C.F.R. §§ 1.56 and 1.97 through 1.98, applicant wishes to make known to the Patent and Trademark Office the references set forth on the attached form PTO/SB/08. This application relies, under 35 U.S.C. § 120, on the earlier filing date of prior Application No. 09/497,855, filed February 4, 2000 (now U.S. 6,604,432). The references listed on the attached form PTO/SB/08 were submitted to and/or cited by the Patent and Trademark Office in this prior application. As to any reference supplied, applicant does not admit that it is "prior art" under 35 U.S.C. §§ 102 or 103, and specifically reserves the right to traverse or antedate any such reference, as by a showing under 37 C.F.R. § 1.131 or other method. Although the aforesaid references are made known to the Patent and Trademark Office in

compliance with applicant's duty to disclose all information he/she is aware of which is believed relevant to the examination of the above-identified application, applicant believes that his/her invention is patentable.

Please acknowledge receipt of this Information Disclosure Statement and kindly make the cited references of record in the above-identified application. No fee is deemed due, but if necessary, the Commissioner is authorized to charge any additional fees due and to credit any overpayments to Deposit Account No. 04-0258 of Davis Wright Tremaine LLP. A copy of this sheet is enclosed.

Respectfully submitted,

DAVIS WRIGHT TREMAINE I

By

Barry L. Davison, Ph.D., Registration No. 47,309

2600 Century Square 1501 Fourth Avenue Seattle, WA 98101-1688 Phone: (206) 622-7621

Facsimile: (206) 628-7699

MAR 2 9 7006 W

PTO/SB/08A (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Representation unless it contains a valid OMB control number.

s, est Sept	Substi	tute for form 1449/PTC)			Complete if Known		
	1,438			2. 4		Application Number	10/081,327	
	IN	ORMATIO	N(D)	SCLO	SURE	Filing Date	02-21-2002	
	ST	ATEMENT-	BY /	APPI I	CANT	First Named Inventor	Huang	
		(Use as many sh	57-57 A		THE PROPERTY OF THE PROPERTY O	Art Unit	1634	
		् (Use as many sn	eets as r	recessary)		Examiner Name	Jeanine Anne Goldberg	
S	heet	1	of	2		Attorney Docket Number	40629-2	

翻片的树			U.S. PATENT			
Examiner Initials*	Cite No. 1	Document Number	Publication Date	Name of Patentee or	Pages, Columns, Lines, Where Relevant Passages or Relevant	
muas	140.	Number-Kind Code ^{2 (if known)}	MM-DD-YYYY	Applicant of Cited Document	Figures Appear	
	A1	US-4,682,195	07-21-1987	Yilmaz		
	A2	US-4,683,202	07-28-1987	Mullis		
	АЗ	US-4,800,159	01-24-1989	Mullis et al.		
	A4	US-5,589,339	12-31-1996	Hampson et al.		
	A5	US-5,591,575	01-07-1997	Hampson et al.		
	A6	US-5,786,146	07-28-1998	Herman et al.		
	A7	US-5,871,917	02-16-1999	Duffy		

	FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No. 1	Foreign Patent Document Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T⁵			

	Cita	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine,	Т
Examiner Initials*	Cite No. ¹	journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Ľ
	A8	AKOPYANTS et al., "PCR-based Subtractive Hybridization and Differences in Gene Content Among Strains of Helicobacter pylon", Proc. Natl. Acad. Sci. USA, Vol. 95, pp. 13108-13113, 1998	L
	A9	ANTEQUERA, F., et al., "High Levels of De Novo Methylation and Altered Chromatin Structure at CpG Islands in Cell Lines", Cell, Vol. 2, pp. 503-514, 1990	
	A10	BAYLIN et al., "Alterations in DNA Methylation: A Fundamental Aspect of Neoplasia", Advances in Cancer Research, pp. 140-196, 1998	
	A11	BAYLIN, STEPHEN B., "Tying it all Together: Epigenetics, Genetics, Cell Cycle, and Cancer", Science, Vol. 277, pp. 1948-1949, 1997	L
	A12	BELINSKY et al., "Aberrant Methylation of p16 ^{INK4a} is an Early Event in Lung Cancer and a Potential Biomarker for Early Diagnosis", Proc. Natl. Acad. Sci. USA, Vol. 95, pp. 11891-11896, 1998	L
	A13	BELINSKY et al., "Increased Cytosine DNA-methyltransferase Activity is Target-cell-specific and an Early Event in Lung Cancer", Proc. Natl. Acad. Sci. USA, Vol. 93, pp. 4045-4050, 1996	
	A14	BLOOM, H.J.G. AND RICHARDSON, W.W., "Histological Grading and Prognosis in Breast Cancer", British Journal of Cancer, Vol. 11, pp. 359-377, 1957	
	A15	BRANDEIS, M. et al., "Sp1 Elements Protect a CpG Island from de novo Methylation", Nature, Vol. 371, pp. 435-438, 1994	
	A16	CAROTTI et al., "Influence of Pre-existing Methylation on the de Novo Activity of Eukaryotic DNA Methyltransferase", Biochem. J., Vol. 37, pp. 1101-1108, 1998	
	A17	CHRISTMAN et al., "5-Methyl-2'-deoxycytidine in single-stranded DNA can act in cis to Signal de novo DNA Methylation", Proc. Natl. Acad. Sci., USA, Vol. 92, pp. 7347-7351, 1995	
	A18	CHUANG et al., "Human DNA-(Cytosine-5) Methyltransferase-PCNA Complex as a Target for p21WAF1", Science, Vol. 277, pp. 1996-2000, 1997	
	A19	CRAIG et al., "Removal of Repetitive Sequences from FISH Probes Using PCR-Assisted Affinity Chromatography", Hum. Genet., Vol. 100, pp. 472-476, 1997	
	A20	CROSS et al., "Purification of CpG Islands Using a Methylated DNA Binding Column", Nature Genet., Vol. 6, pp. 236-244, 1994	
	A21	FROMMER, M. et al., "A Genomic Sequencing Protocol that Yields a Positive Display of 5-Methylcytosine Residues in Individual DNA strands", Proc. Natl. Acad. Sci. USA, Vol. 89, pp. 1827-1831, 1992	
	A22	GRAFF et al., "Mapping Patterns of CpG Island Methylation in Normal and Neoplastic Cells Implicates Both Upstream and Downstream Regions in <i>de Novo</i> Methylation", J. Biol. Chem., Vol. 272, No. 35, pp. 22322-22329, 1997	

1AR 2 9 2006

Substitute for form 1449/PTO

INFORMATION DISCLOSE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

2 Sheet

Complete if Known			
Application Number	10/081,327		
Filing Date	02-21-2002		
First Named Inventor	Huang		
Art Unit	1634		
Examiner Name	Jeanine Anne Goldberg		
Attorney Docket Number	40629-2		

Examiner Initials*	Cite No. 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T²
	A23	HERMAN et al., "Methylation-specific PCR: A Novel PCR Assay for Methylation Status of CpG Islands", Proc. Natl. Acad. Sci. USA, Vol. 93, pp. 9821-9826, 1996	
	A24	HUANG, T.H., et al., "Methylation Profiling of CpG Islands in Human Breast Cancer Cells", Human Molecular Genetics, Vol. 8, No. 3, pp. 459-470, 1999	
	A25	JONES, P.A., "DNA Methylation Errors and Cancer", Cancer Res., Vol. 56, pp. 2463-2467, 1996	
	A26	LAIRD et al., "DNA Methylation and Cancer", Hum. Mol. Genet., Vol. 3, pp. 1487-1495, 1994	
-	A27	LEE J.H. and WELCH D.R., "Identification of Highly Expressed Genes in Metastasis-Suppressed Chromosome 6/Human Malignant Melanoma Hybrid Cells Using Subtractive Hybridization and Differential Display", Int. J. Cancer, Vol. 71, pp. 1035-1044, 1997	
	A28	LI et al., "Role for DNA Methylation in Genomic Imprinting", Nature, Vol. 366, pp. 362-365, 1993	
	A29	MUMMANENI, P., et al., "Epigenetic Gene Inactivation Induced by a Cis-acting Methylation Center", J. Biol. Chem., Vol. 270, No. 2, pp. 788-792, 1995	
	A30	PFEIFER, G.P., et al., "Polymerase Chain Reaction-Aided Genomic Sequencing of an X Chromosome-linked CpG Island: Methylation Patterns Suggest Clonal Inheritance, CpG Site Autonomy, and an Explanation of Activity State Stability", Proc. Natl. Acad. Sci. USA, Vol. 87, pp. 8252-8256, 1990	
	A31	SAIKI et al., "Primer-Directed Enzymatic Amplification of DNA with a Thermostable DNA Polymerase", Science, Vol. 239, pp. 487-491, 1988	
	A32	SCHENA et al., "Quantitative Monitoring of Gene Expression Patterns with a Complementary DNA Microarray", Science, Vol. 270, pp. 467-470, 1995	
	A33	SINGER-SAM, J. and RIGGS, AD., "X-Chromosone Inactivation and DNA Methylation", DNA Methylation: Molecular Biology and Biological Significance, pp. 358-384, 1993	
	A34	VERTINO et al., "De Novo Methylation of CpG Island Sequences in Human Fibroblasts Overexpressing DNA (Cytosine-5) – Methyltransferase", Mol. Cell Biol., Vol. 16, pp. 4555-4565, 1996	
	A35	WU et al., "Expression of Prokaryotic <i>Hha</i> l DNA Methyltransferase is Transforming and Lethal to NIH 3T3 Cells", Cancer Res., Vol. 56, pp. 616-622, 1996	

Examiner	Date	
Signature	Considered	

*EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609. Draw line through citation if not in conformation and not considered. Include copy of this form with next communication to applicant.

not considered. Include copy of this form with next communication to applicant.

Applicant's unique citation designation number (optional). Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to compete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 (1-800-786-9199) and select option 2.